Naval Medical Research Unit Dayton
Wright-Patterson AFB, Ohio

Science Update

Volume 5, Issue II Spring

MISSION

To maximize warfighter performance and survivability through premier aeromedical and environmental health research-delivering solutions to the field, the Fleet, and for the future.

VISION

NAMRU-D is Navy Medicine's world class, global aeromedical and toxicology research leader. Our efforts and innovative products are aligned with operational requirements to solve the naval and joint warfighter challenges of the future.

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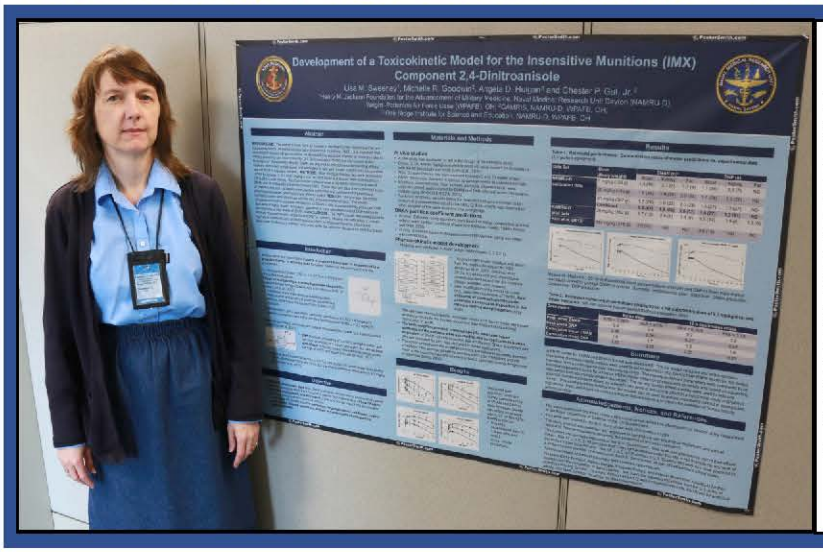
NAMRU-D Presents at the 54th Annual Meeting of the Society of Toxicology: Alternative Jet Fuel and Insensitive Munitions Research



Dr. Lisa Sweeney presented her research on the Development of a Toxicokinetic Model for Insensitive Munitions (IMX) Component 2, 4-Dinitroanisole at the 2015 Society of Toxicology (SOT) held March 22 - 26 in San Diego, CA. Dr. Sweeney is a Senior PBPK Toxicologist at NAMRU-D and has attended the annual SOT meeting since 1995.

By: Dr. Lisa Sweeney

Scientists from Naval Medical Research Unit Dayton's (NAMRU-D) Environmental Health Effects Directorate attended and presented research during the 54th Annual Meeting of the Society of Toxicology (SOT) held in San Diego, CA March 22 to 26, 2015. This meeting brings together approximately 6,900 toxicologists from over 50 countries to discuss recent advances and technologies in toxicological research. Dr. Karen Mumy, Dr. Lisa Sweeney, LCDR Jennifer Mueller and LCDR Carlis Brown attended from NAMRU-D. Dr. Sweeney chaired a platform session on applications of ToxCast/Tox21 data. Dr. Sweeney and Dr. Mumy were authors or co-authors on two poster presentations, both of which described efforts done in conjunction with Department of Defense partners.

NAMRU-D scientists teamed up with 711th Human Performance Wing/RHDJ U.S. Air Force scientists for an evaluation of the potential effects of "Alcohol-to-Jet" (ATJ) alternative jet fuels. The authors determined that the appropriate occupational exposure limits for these fuels are equivalent to those for traditional Air Force jet fuel (that is, JP-8). Dr. Mumy and Dr. Sweeney of NAMRU-D were co-authors of this work which was presented during a poster session entitled, "Toxicity of Chemical Mixtures."

In collaboration with U.S. Army, Dr. Sweeney presented a poster entitled, "Development of a toxicokinetic model for the insensitive munitions (IMX) component 2,4-dinitroanisole (DNAN)," in a session focused on Biological Modeling. IMX formulations are less susceptible to unintentional detonation than conventional munitions, but their potential hazard to humans is unknown. Scientists at NAMRU-D conducted laboratory studies to evaluate the absorption, distribution, metabolism, and elimination of DNAN and its more toxic metabolite2,4-dinitrophenol (DNP) in rats. These data and similar data generated by the Army for nonhuman primates (rhesus macaques) were used by Dr. Sweeney to develop preliminary physiologically based pharmacokinetic (PBPK) models of DNAN and DNP in rats, macaques, and (by extrapolation) humans. The PBPK model was used to generate estimated human no-effect exposure levels for DNAN based on no-observed adverse effect levels determined in laboratory animals. The human no-effect levels may be used to guide the selection of occupational and environmental exposure limits for DNAN.

Investigating Chemical Exposure at High Altitudes in High Performance Aircraft

Left to right: Dr. Deidre Mahle, Mr. Richard James, and LCDR Carlis Brown have been collaborating to investigate chemical exposure at high altitudes in high performance aircraft.

By: LCDR Carlis Brown & Dr. Deirdre Mahle (U.S. Air Force 711 HPW/RHDJ)

The USAF has been identifying potential contributing factors to episodes of suspect hypoxia seen in pilots during training missions. In-flight emergencies with high performance aircraft indicate a gap in our knowledge or understanding of stressors in the environment and impact on physiology and/or toxicology. The 711th Human Performance Wing (HPW), Molecular Bioeffects Branch has teamed with NAMRU-D to further investigate identified data gaps for chemical exposure at high altitudes. One of the uncertainties is the effects of volatile organic chemicals (VOCs) that have been detected as a cockpit contaminant, of which toluene is one example. Toluene is a chemical with a good scientific exposure database that can easily be measured in blood and tissues and it has a known physiologically based pharmacokinetic (PBPK) model for the human exposure as well as a corollary PBPK model for a rat. In addition, toluene has been shown to have a link to hypoxia in some studies which increases its relevance to this study. NAMRU-D was asked to develop a system that could simulate the inhalation exposure of toluene at high altitudes in an animal model. Such a system would duplicate conditions experienced in flight and allow the AF to determine whether or not changes in altitude will significantly increase the uptake of VOCs compared to exposures at normal ambient atmospheres.

NAMRU-D Attends 2015 Shoresh Working Group Meeting in Israel

By: CDR Michael Lowe

On March 13-21, 2015 members of Naval Medical Research Unit Dayton's (NAMRU-D) Aeromedical scientific research staff attended and presented at the Shoresh Working Group Meeting in Ramat Gan, Israel as invited members of the U.S. Department of Defense/Israeli Defense Forces Aeromedical Working Group. CDR Michael Lowe, Head, Biomedical Science Department, NAMRU-D and Dr. Michael Reddix, Senior Research Psychologist at NAMRU-D, presented three of the four NAMRU-D briefs during the 17th Shoresh meeting. Dr. Richard Arnold, Aeromedical Research Director, NAMRU-D phoned in to the meeting to present NAMRU-D's command overview. This is the first Shoresh meeting to include the U.S. Air Force and U.S. Navy and also the first to look at aeromedical research priorities. Various topics and issues regarding challenges of operating in the extreme aerospace environment were discussed. Dr. Reddix covered Simulation of Aviation Illusions and Advanced Computerized Color Vision Screening. NAMRU-D's hypoxia research, specifically exposure sequel, recovery and mask based sensors was presented my CDR Lowe. The hypoxia brief included accomplishments with initial collaborations in foreign comparative testing featuring the Israeli company Elbit. This work presents a solid starting point for future collaborations in hypoxia and other aeromedical domains is the current the U.S. and Israel joint effort investigation on mask sensors in hypoxia.

NAMRU-D's fatigue laboratory, Disorientation Research Device, various cognitive tests, EEG capabilities, and other physiological measures provide considerations for future jointness. In fact, at the end of the meeting the Aeromedical topics for possible collaboration and inclusion in the final working group document for action items were produced, prioritized, and presented to the Surgeon Generals on the last day. Three NAMRU-D centric topics made the list of 11 items of which CDR Lowe is the NAMRU-D point of contact for each. These focal areas were: 1) Spatial Disorientation, 2) Hypoxia, and 3) Fatigue.

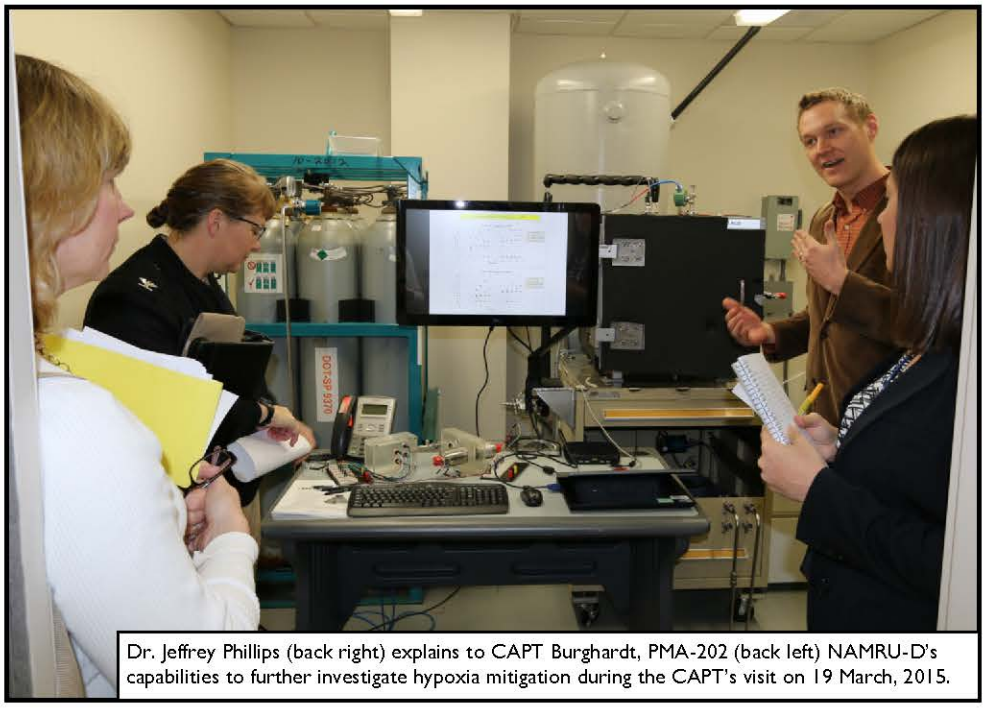
CDR Lowe and Dr. Reddix at a function during the 2015 Shoresh Working Group Meeting .

As a result of the meeting the foundation is being laid through mutually beneficial information exchanges and potential research collaborations with no expectation for funding exchanges. . NAMRU-D's attendance at the working group symbolized the first step in forming a collaborative relationship with Aeromedical entities in Israel and significantly builds upon the foundations of the prior joint work on hypoxia sensors with Elbit. CDR Lowe strongly recommended that NAMRU-D attend the next Shoresh Working Group and further commits to this working group fully in the future with an even larger contingent.

NAMRU-D Continues to Investigate Hypoxia Mitigation

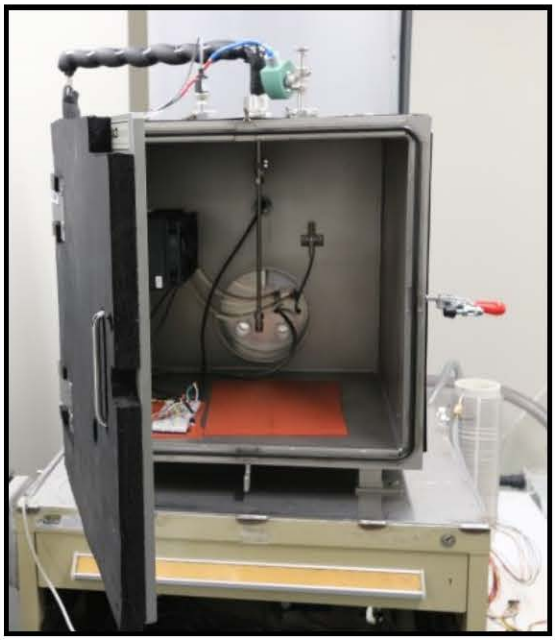
By: Dr. Jeffrey Phillips

Naval Medical Research Unit Dayton's hypoxia laboratory focuses both on quantifying the performance effects of hypoxia and identifying emerging technologies to provide fail-safe hypoxia mitigation. The hypoxia lab is staffed with experimental psychologists, physiologists, and biomedical engineers. NAMRU-D Investigators have executed numerous studies evaluating off-the-shelf biomedical sensors for their ability to reliably detect an impending hypoxic threat before the operator experiences significant performance degradation. Technologies evaluated include near infrared spectroscopy, pulse oximetry, reflectance pulse oximetry, eye tracking, and pupilometry.



Dr. Jeffrey Phillips (back right) explains to CAPT Burghardt, PMA-202 (back left) NAMRU-D's capabilities to further investigate hypoxia mitigation during the CAPT's visit on 19 March, 2015.

Both the Air Force and Navy are currently developing in-mask gas sensor suites to provide warnings to aviators when a life support malfunction occurs. Unfortunately, most commercial gas sensors do not perform well in tactical aviation environments due to the large variations in barometric pressure, humidity, and temperature. NAMRU-D houses a state-of-the-art gas sensor testing facility which allows gas and chemical sensors to be evaluated in conditions equivalent to the flight environment. Sensors are tested in a hypobaric chamber while pressure, humidity and temperature are manipulated. To date, twenty-two sensors have been evaluated in our facility. This testing has verified that sensor sensitivity and specificity improvements are still required before they can reliably provide significant hypoxia mitigation in-flight.



Small Hypobaric Environmental Chamber for sensor testing in aviation-relevant environmental conditions. The chamber can vary pressure, temperature, humidity, & airflow on sensors of interest.

The NAMRU-D hypoxia team has also conducted multiple studies to model the onset of hypoxia performance effects as well as the recovery of performance following hypoxia exposure. Breaking with traditional teaching, NAMRU-D study results suggest that operators exposed to hypoxic environments experience significant performance degradation at a much earlier time point than predicted by the Time of Useful Consciousness Tables customarily used for risk assessments. Furthermore, previously unappreciated subtle performance effects have been found to persist for hours following exposure. The most recent study also found empirical evidence of an oxygen paradox as subjects experienced the largest performance deficits while they were being administered a five minute treatment with 100% oxygen following hypoxia exposure. This implies that following hypoxia exposure, operators could remain significantly impaired throughout the remainder of the flight.

In the coming years, the NAMRU-D hypoxia lab will continue to conduct experiments to better understand the performance effects of hypoxia, to test hypoxia-mitigation sensors for their ability to perform in the tactical flight environment, and to identify a hypoxia recovery gas mixture that will provide quick recovery from hypoxia exposure without further compromising performance.

NAMRU-D's Visitors

03.19.2015. CAPT Andrews, NAMRU-D Commanding Officer (left) introduced Brigadier General Payne, AFMOA (right) to NAMRU-D's Disorientation Research Device. CDR Folga (2nd on right) briefed the devices capabilities. Brigadier General Timothy Jex, 711 Human Performance Wing Commander (center) accompanied Brigadier General Payne's tour.

04.23.2015. CDR Folga highlights the Disorientation Research Device's future applications for the safety of the war fighter to Environmental Tectonics Corporation ETC Board of Directors.

03.19.2015. Dr. Jeffrey Phillips demonstrates the functions of the head mounted sensors connected to an Reduced Oxygen Breath Device to CAPT Burghardt, PMA-202 during a visit to the NAMRU-D facilities.

04.23.2015. NAMRU-D hosted a visit from Environmental Tectonics Corporation (ETC) Board of Directors to observe a motion demonstration of NAMRU-D's Disorientation Research Device. Left to right: CAPT Lee, XO; H. F. "Gerry" Lenfest, Chairman of the Board of Directors; CAPT Andrews, CO; Robert L. Laurent, Jr., Chief Executive Officer and President; CDR Folga; and Winston E. Scott, Director. Right to left: Linda J. Brent; Director and Roger Colley, Director.

NAMRU-D Products & Presentations

Becker, W.J., Geyer, D.J., Gomez, K., & Littman, E.M. (2015, May). *Pharmacokinetics and Efficacy of Intranasal Scopolamine Spray.* Poster presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Bradley, J.L., Reddix, M.D., Folga, R.V., & Tapia, M.L. (2015, May). *Laser-Pointer Illumination Events in Naval Aviation Operations.* Presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Caldwell, J.A. & Caldwell, J.L (2015, May). *Understanding and managing fatigue in aviation.* Workshop at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Caldwell, J.L. (2015, May). *The evidence base for use of modafinil to mitigate fatigue.* Workshop at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Caldwell, J.L. (2015, May). *Aviation Fatigue Countermeasures Pat II: Advances in Fatigue Management.* Workshop at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Drummond, L.A., Funke, M.G., Phillips, J.B., Robinson, F.E., Warner, S.W., Geyer, D.J., & Gomez, J. (May, 2015). *Recovery from Hypoxic Exposure.* Presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Funke, M.G., Gomez, J., Phillips, J.B., Lee, M.C., Wright, & Becker, W.J. (2015, May). Performance *Costs Associated with Modifications to the Oxygen Delivery Schedule of the On-Board Oxygen Generating System.* Poster presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Gao, H., Reddix, M.D., & Kirkendall, C. (2015, May). *Can Operationally-relevant accuracy and reaction-time metrics guide the development of color-vision standards?.* Presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Hartzler, B.M. (March, 2015). Predicting performance during chronic sleep loss: Identification of factors sensitive to individual fatigue resistance. Technical Report retrieved from Defense Technical Information Center.

Hartzler, B. M., Chandler, J.F., & Levin, C.B.S. (2015, May). *Identification of measures and moderators to improve prediction of impairments due to chronic sleep loss.* Poster presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Littman, E.M., Lawson, B., Brill, J.C., & Rupert, A. (May, 2015). *Near-Future Technological Countermeasures for Spatial Disorientation in Flight.* Presentation at International Symposium on Aviation Psychology.

McGowan, K.J., Gao, H., & Whitwell, K.J. (May, 2015). *United States Naval Aerospace Optometry.* Presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Patterson, F.R., Williams, H.P., Arnold, R.D, & Folga, R.V. (May, 2015). Aviator Black Hole Illusion: Validation Training Countermeasures for Newly Identified Causal Factors. Presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Phillips, J.B., Robinson, F.E., Drummond, L. A., & Funke, M.G. (May, 2015). *Time of Useful Performance: A Complement to the Time of Useful Consciousness Table.* Presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Phillips, J.B., Grigsby, C., Mayes, R., & Tripp, L. (May, 2015). *In-Flight Hypoxia: From Sensors to Biomarkers.* Presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Sweeney, L.M., Sommerville, D.R., Channel, S.R., Sharits, B.C., Gargas, N.M., and Gut, C.P., Jr. (2015). Evaluating the validity and applicable domain of the toxic load model: impact of concentration vs. time profile on inhalation lethality of hydrogen cyanide. Regul. Toxicol. Pharmacol. 71:571-584.

Williams, H.P., Littman, E.M., Folga, R.V., & Patterson, F.R. (May, 2015). *Field of view evaluation for flight simulators used in spatial disorientation training.* Presentation at 85th Annual Aerospace Medicine Association Conference, Orlando, Florida.

Commanding Officer's Corner

Captain Jeffrey M. Andrews, MSC, USN
Commanding Officer

It is now just past Memorial Day as I write this spring edition and the opportune time to reflect on our fallen warriors and their ultimate sacrifice. Our mission is all about them. Let their death be not in vain, but a spark to ignite motivation to make the future better and safer for those in harms way. All 75 personnel at NAMRU-D know their unique mission, but even more importantly there is a collective understanding and selfless commitment that we exist for the joint warfighter. All of our science and efforts are aligned with operational requirements and our products can and do make a difference in the performance and survivability of those on the battlefield. Even basic Research & Development (R&D) can be the foundation for a future cutting edge solution in any operational setting.

Despite the obstacles of bureaucracy, over-regulation, and limited/uncertain funding, successful R&D starts with an idea. At NAMRU-D, our scientists have ideas that are based on fleet experience and operational input. That idea needs to be fueled not only by passion and persistence, but will have to grow and ideally be put to use in an operational setting and applied by the warfighter. It is during this growth phase that our scientists sprinkle on some intellect, creativity, teamwork, jointness, collaboration, and yes a touch of luck to finish the main course and satisfy the appetite of our eaters in the fleet.

This Science Update covers only a 3 month snapshot of life at NAMRU-D and showcases some of our toxicological and aeromedical accomplishments, international involvement with Israel, and the constant, high visible tours of VIPs and high ranking officials and agencies. What is not covered is the mindset, motivation, and professionalism of the NAMRU-D team that make the R&D into a way of life with the pursuit of that product or system that will ultimately reach the warfighter and maybe someday save lives. I salute those who died for our freedom and commend those who commit their lives to R&D in support of our heroes. NAMRU-D stands ready for ideas, sound science, and continued growth of capabilities to support our nation's finest.

Taking the Helm of Navy Medicine's Aeromedical & Environmental Health Research

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